AMENDMENTS TO THE SPECIFICATION:

Please replace paragraph [0005], at page 1, with the following amended paragraph:

--**[0005]** The process of lateral inhibition prevents neighboring cells from developing into the same type of differentiated cells in flies and in vertebrates. *See* Tanabe & Jessell, *Science*, 274:1115-23 (1996). In Drosophila, a group of mutations has been described that shows severe defects in the process of lateral inhibition in the developing nervous system. These neurogenic mutations result in hyperplasia of the neural tissue at the expense of epidermal structures. *See* Campos-Ortega & Jan, *Annu Rev Neurosci*, 14:399-420 (1991). The temporal and spatial expression patterns of [[the]] neu are compatible with its function as a neurogenic gene in Drosophila. The Neu protein is expressed throughout the ectoderm at the time when cell fate is determined and its expression proceeds in neuroblasts. *See* Boulianne, *et al.*, *EMBO J*, 10:2975-2983 (1991). neu expression has been detected in actively proliferating neuroblasts in several regions of the central nervous system (CNS) [[CNS]] and peripheral nervous system (PNS) [[PNS]]. Expression of neu in imaginal disc suggests that it is also involved in later stages of development. The neu gene encodes a RING finger (C3HC4) type zinc finger protein. The molecular function of the Drosophila Neu protein is unknown. Interestingly, it was discovered that EST ~~data bases~~ databases contain a homologue of Neu suggesting that a family of Neu-like proteins is present in Drosophila.--

Please replace paragraph [0031], at page 2, with the following paragraph:

--**[0031]** Mammalian Neu1 acts as a powerful transcriptional repressor in transient expression assays and silences both [[,]] TATA-containing and TATA-less promoters, including the promoters of the nerve growth factor (NGF) [[NGF]], brain-derived neurotrophic factor [[BDNF]], neurofilament light chain [[NF-L]], and growth-associated protein-43 genes [[GAP-43]]. Neuralized homology repeat domains (NHRs) [[NHRs]] function as transcription repression domains, suggesting that NHR-containing proteins represent a novel class of transcriptional repressors. It is likely that mammalian Neu1 mediates transcriptional repression through protein-protein interactions. Like several known repressors, mammalian Neu1 could function

through interaction with co-repressors such as dCtBP or mammalian homologues of Groucho, and general repressor complexes, such as NC2, Mot1, or Not to interfere with the function of Pol II complex. See Maldonado *et al.*, *Cell*, 99:455-458 (1999) and Mannervik *et al.*, *Science*, 284:606-609 (1999). Alternatively, repression could be achieved through chromatin remodeling by recruiting the histone deacetylase complexes (HDACs). See Glass and Rosenfeld, *Endocr Rev*, 21:447 (2000); Knoepfler and Eisenman, *Cell*, 99:447-450 (1999); and Torchia *et al.*, *Curr Opin Cell Biol*, 10:373-383 (1998). Current data suggest that the mechanism of Neu1 repression does not include a HDAC complex in neuroblastoma Neuro2A cells, as the HDAC inhibitor trichostatinA did not relieve m-Neu1-mediated repression in these cells.--

Please replace paragraph [0033], at page 2, with the following amended paragraph:

--**[0033]** A putative nuclear localization signal (NLS) has been identified in the N-terminus of d-Neu, however, the NLS sequence identified in d-Neu [[,]] is not conserved in mouse, rat and human Neu proteins. See Boulianne *et al.*, *EMBO J.* 10:2975-2983 (1991) and Price *et al.*, *EMBO J*, 12:2411-2418 (1993). The weak NLS sequences (HKAVKR (SEQ ID NO: 43), RLKITKK (SEQ ID NO: 44)), that were identified in mammalian Neu1 proteins, have been suggested to regulate nuclear import of a fraction of the synthesized protein. See Boulikas, *J Cell Biochem*, 60:61-82 (1996). Indeed, m-Neu1 resides both in the cytoplasm and in the nucleus, revealing that it is the subject of regulated nuclear import. Recent studies have shown that importin-α family members are involved in the formation of the NLS receptor complexes that govern the protein transport to the nucleus. See Ullman *et al.*, *Cell*, 90:967-970 (1997); and Izaurralde and Adam, *RNA*, 4:351-364 (1998). Interestingly, importin-α3 was identified here as one of the m-Neu interacting proteins by yeast two-hybrid screening. Furthermore, the results discussed herein also demonstrate that the CRM1/exportin1-related export pathway controls the nucleocytoplasmic shuttling of Neu1, since the nuclear export of a tagged-m-Neu1 fusion protein is blocked by LMB. LMB is a microbial metabolite that inactivates the nuclear export by interfering with the binding of CRM1/exportin1 to the nuclear export signals. See Fornerod *et al.*, *Cell*, 90:1051-1060 (1997); Kudo *et al.*, *Exp Cell*

Res, 242:540-547 (1998); Kudo *et al.*, *Proc Natl Acad Sci USA*, 96:9112-9117 (1999); Fukuda *et al.*, *Nature*, 390:308-311 (1997); and Nishi *et al.*, *J Biol Chem*, 269:6320-6324 (1994). These data reveal that mammalian Neu1 function is additionally regulated by nucleocytoplasmic shuttling.--

Please replace paragraph [0071], at page 6, with the following amended paragraph:

--**[0071]** Representative polynucleotide molecules encoding members of the Neu family include sequences comprising ~~SEQ. ID. NOs.:~~ SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, and 33. Polynucleotide molecules encoding Neu family members include those sequences resulting in minor genetic polymorphisms, differences between species, and those that contain amino acid substitutions, additions, and/or deletions.--

Please replace paragraph [0075], at page 6, with the following amended paragraph:

--**[0075]** neu family polynucleotide molecules can be isolated using standard hybridization techniques with probes of at least about 7 nucleotides in length and up to and including the full coding sequence. Other members of the neu family can be identified using degenerate oligonucleotides capable of hybridization based on the sequences disclosed herein for use PCR amplification or by hybridization at moderate or greater stringency. The term, "capable of hybridization" as used herein means that the subject nucleic acid molecules (whether DNA or RNA) anneal to an oligonucleotide of 15 or more contiguous nucleotides of ~~SEQ. ID. NOs.:~~ SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, [[and]] or 33.--

Please replace paragraph [0078], at page 6, with the following amended paragraph:

--**[0078]** Alternatively, polynucleotides having substantially the same nucleotide sequence set forth in ~~SEQ. ID. NOs.:~~ SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, and 33 or functional fragments thereof, or nucleotide sequences that are substantially identical to ~~SEQ ID NOs:~~ SEQ ID NO:1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, and 33, can represent members of the Neu family of

proteins. By "substantially the same" or "substantially identical" is meant a nucleic acid or polypeptide exhibiting at least 80%, 85%, 90%, 95% or 100% homology to a reference nucleic acid. For nucleotide sequences, the length of comparison sequences will generally be at least 10 to 500 nucleotides in length. More specifically, the length of comparison will be at least 50 nucleotides, at least 60 nucleotides, at least 75 nucleotides, and at least 110 nucleotides in length. --

Please replace paragraph [0079], at page 6, with the following amended paragraph:

--**[0079]** One embodiment of the invention provides isolated and purified polynucleotide molecules encoding Neu proteins, wherein the polynucleotide molecules that are capable of hybridizing under moderate to stringent conditions to an oligonucleotide of 15 or more contiguous nucleotides of ~~SEQ. ID. NOs.:~~ SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, [[and]] or 33, including complementary strands thereto.--

Please replace paragraph [0099], at page 9, with the following amended paragraph:

--**[0099]** According to the present description, polynucleotide molecules encoding Neu encompass those molecules that encode Neu proteins or peptides that share identity with the sequences shown in ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34. Such molecules preferably share greater than 30% identity at the amino acid level with the disclosed sequences in Neu. In preferred embodiments, the polynucleotide molecules can share greater identity at the amino acid level across highly conserved regions such as the neuralized homology repeat domains and the RING-zinc finger domains.--

Please replace paragraph [0100], at page 9, with the following amended paragraph:

--**[0100]** It is contemplated that amino acid sequences substantially the same as the sequences set forth in ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, are encompassed by the described invention. A preferred embodiment includes polypeptides having substantially the same

sequence of amino acids as the amino acid sequence set forth in ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, or functional fragments thereof, or amino acid sequences that are substantially identical to ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34. By "substantially the same" or "substantially identical" is meant a polypeptide exhibiting at least 80%, preferably 85%, more preferably 90%, and most preferably 95% homology to a reference amino acid sequence. For polypeptides, the length of comparison sequences will generally be at least 16 amino acids, preferably at least 20 amino acids, more preferably at least 25 amino acids, and most preferably 35 amino acids.--

Please replace paragraph [0102], at page 9, with the following amended paragraph:

--**[0102]** The term "functional fragments" ~~include~~ includes those fragments of ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34, or other Neu family members, that retain the function or activity of a Neu transcriptional regulator. One of skill in the art can screen for the functionality of a fragment by using the examples provided herein, where full-length Neu transcriptional factors are described. It is also envisioned that fragments of various Neu proteins that inhibit or promote transcription can be identified in a similar manner. Neu transcriptional activity can also be assayed by standard transcription assays. --

Please replace paragraph [0109], at page 10, with the following amended paragraph:

--**[0109]** One embodiment of the present invention involves the isolation of proteins that interact with Neu proteins and regulate Neu protein function or are regulated by Neu. Neu proteins can be used in immunoprecipitation to isolate interacting factors or used for the screening of interactors using different methods of two hybrid screening. Isolated interactors of Neu can be used to modify Neu activity or Neu can be used to modify the activity of interactors. Two hybrid screening has resulted in the isolation of several types of interactors. Sequence analyses showed that all interactors are novel proteins and contain RING-zinc finger domain located in the C-

terminus of the protein. Neul-1 (4 clones) is a novel splice variant (~~SEQ. ID. NOs.:~~ SEQ ID NO: 35, 36) of zinc finger protein Miz1/PIASXα/ARIP3 (GenBank accession numbers NM_008602; AF077953; AF077954; AF044058). Neul-2 (3 clones) is a fourth homolog (~~SEQ. ID. NOs.:~~ SEQ ID NO: 37, 38; GenBank accession ~~number~~ numbers AF277171; AF302084) of zinc finger protein ZNF127 (GenBank accession numbers U19106; U19107). Neul-3 (9 clones) has highest homology to a human hypothetical protein (GenBank accession number AK001459) and to a Drosophila hypothetical protein (AAF56052.2) produced from CG4813 gene of a genomic scaffold (GenBank accession number AE003740) (~~SEQ. ID. NOs.:~~ SEQ ID NO: 39, 40). Neul-4 (12 clones) is the homolog of the androgen receptor coactivator ARA54 (SEQ. ID. NO.: 32; GenBank accession number AF060544) (SEQ. ID. NO.: 41, 42). --

Please replace paragraph [0110], at page 10, with the following amended paragraph:

--**[0110]** In still another embodiment, synthetic peptides, recombinantly derived peptides, fusion proteins, chiral proteins (stereochemical isomers, racemates, enantiomers, and D-isomers) and the like are provided which include a portion of Neu or the entire protein. The subject peptides have an amino acid sequence encoded by a nucleic acid which hybridizes under stringent conditions with an oligonucleotide of 15 or more contiguous nucleotides of ~~SEQ. ID. NOs.:~~ SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, or 33. Representative amino acid sequences of the subject peptides are disclosed in ~~SEQ. ID. NOs.:~~ SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34. The subject peptides find a variety of uses, including preparation of specific antibodies and preparation of antagonists of Neu activity. --

Please replace paragraph [0187], at page 18, with the following amended paragraph:

--**[0187]** A tissue sample is obtained from a subject possibly suffering from a neoplastic disease. The biopsy is removed and cut into less than 2 gram pieces. These pieces are quick-frozen in liquid nitrogen. Twenty (20 ml) of tissue guanidinium solution is used to process 2 grams of tissue. The tissue guanidinium

solution is prepared by dissolving 590.8 grams of guanidinium isothiocyanate in approximately 400 ml DEPC-treated H_2O. To this is added 25 ml of 2M Tris-Cl, pH 7.5 (0.05 M final) and 20 ml of 0.5 M Na_2EDTA, pH 8.0 (0.01 M final). Stir overnight, adjust the volume to 950 ml, and filter. Finally, add 50 ml 2-mercaptoethanol (2-ME) [[2-ME]].--